Competition between Receptors in Dynamic Combinatorial Libraries

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Published in:
Journal of the American Chemical Society

DOI:
10.1021/ja0509026

Publication date:
2005

J. Am. Chem. Soc.

Supporting Information

Competition between receptors in dynamic combinatorial libraries: amplification of the fittest?

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ADDITIONAL DATA

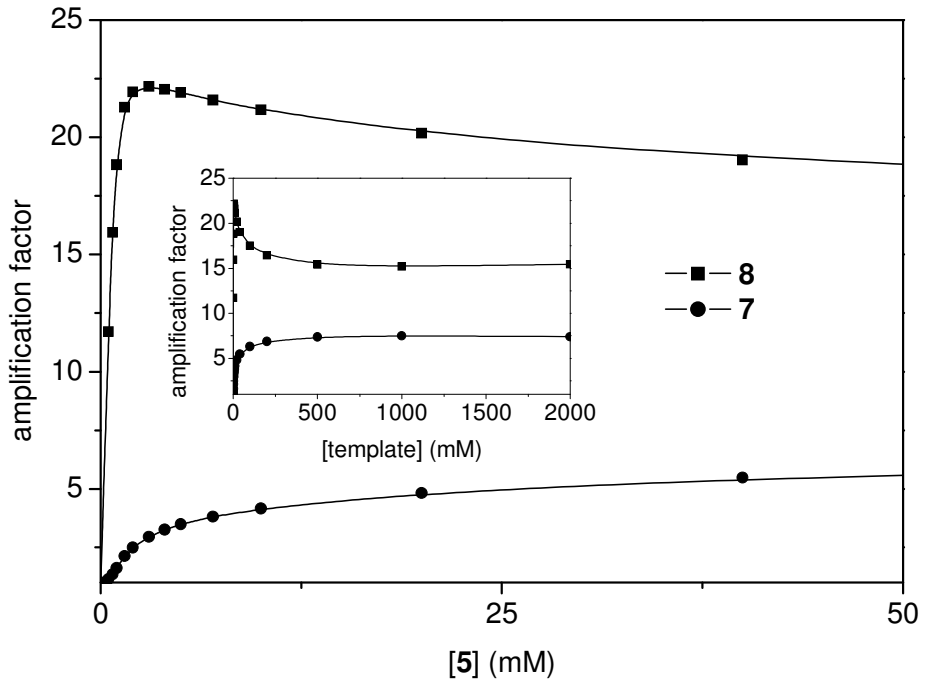

Figure S1. *Simulation results showing amplification factors of* ***7*** *and* ***8*** *as a function of the concentration of guest* ***5*** *for the library in Figure 1c. The inset shows the amplification factors at higher guest concentrations.*

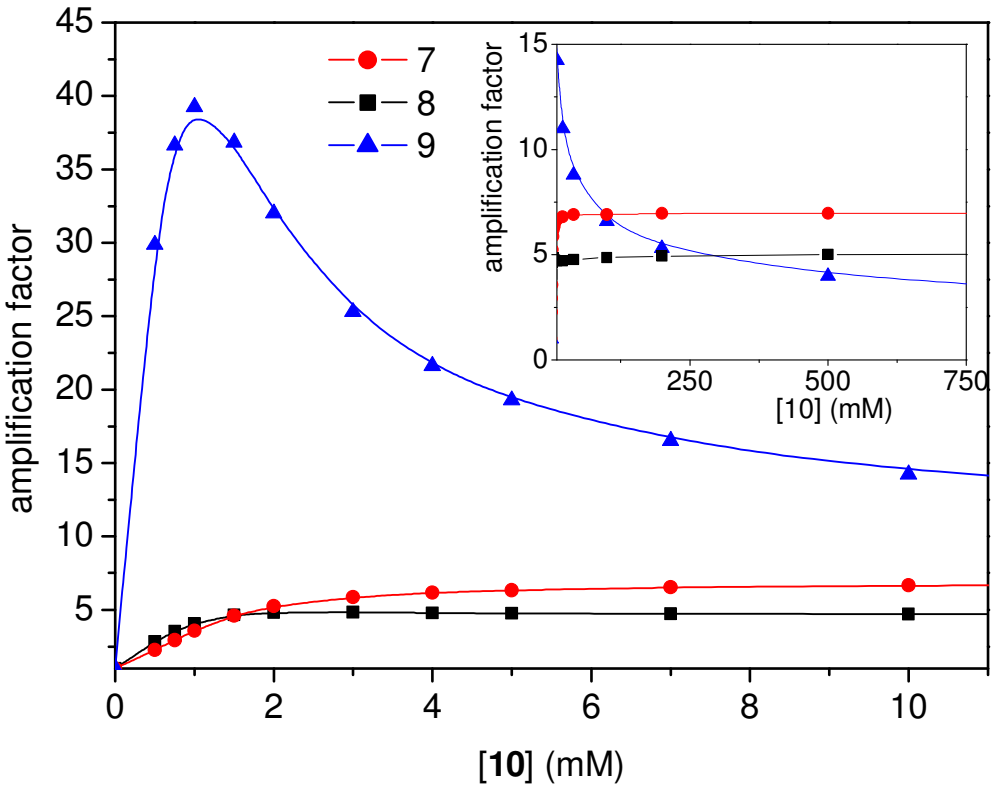

Figure S2. *Simulation results showing amplification factors of* ***7****,* ***8*** *and* ***9*** *as a function of the concentration of guest* ***10*** *in the DCL made from* ***1*** *(3.67mM) and* ***2*** *(1.33mM). The inset shows the amplification factors at higher guest concentrations. Note that at very high template concentrations the amplification factors are in the order* ***7*** *>* ***8*** *>* ***9*** *whereas the binding constants are in the order of* ***9*** *>* ***8*** *>* ***7****.*

Table S1. *Simulated concentrations of **7**, **8** and **9** in the DCL made from **1** (3.67mM) and **2** (1.33mM) as a function of the concentration of guest **10**.*

[**10**] (mM)	[**9**] (mM)	[**8**] (mM)	[**7**] (mM)
0	0.00149	0.0426	0.191
0.50	0.0445	0.120	0.434
0.75	0.0546	0.150	0.560
1.00	0.0585	0.173	0.682
1.50	0.0549	0.198	0.879
2.00	0.0477	0.205	1.00
3.00	0.0377	0.206	1.12
4.00	0.0322	0.204	1.18
5.00	0.0287	0.203	1.21
7.00	0.0246	0.201	1.25
10	0.0212	0.200	1.27
20	0.0164	0.200	1.30
40	0.0131	0.203	1.32
100	0.00981	0.207	1.32
200	0.00791	0.210	1.33
500	0.00594	0.213	1.33
1000	0.00476	0.215	1.33
2000	0.00381	0.216	1.33

EXPERIMENTAL DETAILS

Materials

The synthesis of building blocks **1**[2b], **2**[2b] and **3**[S1] and receptors **7**[2b], **8**[2b] and **9**[2a] and guests **4**[2b], **5**[2b] have been described previously.

Dynamic combinatorial libraries

DLCs were constructed by dissolving the required building blocks **1**-**3** in water, and adjusting the pH to 8 using NaOH and HCl. The resulting solutions (5mM or 10mM) were allowed to equilibrate for at least 2 weeks, either in the absence or presence of the guest, by stirring as 1mL aliquots in closed 2mL HPLC vials.

HPLC conditions for analysis of the DCLs in Figures 1-4.

Conditions for Figure 1a-c are described in ref. 2b. The remaining HPLC analyses were carried out on Hewlett Packard 1050 and 1100 systems coupled to a UV analyzer, set to 320nm. The data were processed using HP Chemstation software. Separations were achieved using a Waters Symmetry C_{18} column (25.0 cm × 4.6 mm, 5 μm particle size).

For Fig. 1d,e and Fig. 2c,d the following gradient was used at a flow rate of 1mL/min, at 45°C, with 2µl injections:

time (min)	% H_2O (0.1% TFA)	% MeCN (0.1% TFA)	% IPA (0.1% TFA)
0	95	4.2	0.8
30	5	79.8	15.2
34	5	79.8	15.2
35	95	4.2	0.8
50	95	4.2	0.8

For Fig 2a,b and 3 the following gradient was used at 1mL/min, 45°C, with 2µl injections:

Time (min)	% H_2O + 0.1% TFA	% MeCN + 0.1% TFA	% IPA + 0.1% TFA
0	50	38	12
30	50	38	12
31	0	76	24
35	0	76	24
36	50	38	12
50	50	38	12

For the data in Fig. 4b an isocratic mobile phase was used at 1mL/min, consisting of acetonitrile, water and trifluoroacetic acid in the ratio of 55:45:0.1. The analysis was performed at room temperature. An injection volume of 2µl was used.

Equilibrium Simulations

Equilibrium calculations were performed using DCLSim 1.1, using the modules that support the calculation of user-specified equilibria. The algorithms used in DCLSim 1.1 are unchanged from DCLSim 1.0 – however, they have been re-coded in C to increase the speed of the simulations. Further details are provided in the supporting information to ref. 4. Please contact the authors for the availability of the software.

The equilibrium models used represent idealized versions of the dynamic combinatorial libraries studied – they do not include isomerism, or any minor template effects that have been observed, and they have not been fitted to experimental peak areas. One adjustment has been made: dimers **1.2** and **2.2** have not been included. This is consistent with the observed experimental behavior of the library, in which those dimers are not formed in significant quantities. Control simulations in which **1.2** and **2.2** were allowed to form gave similar overall results.

The listings below represent the library compositions and equilibrium constants for the formation of the library members from the building blocks (K) and the experimental Gibbs energy of binding of the library members to the guest ($\Delta G°$), used as input for the simulations. The equilibrium constants of formation are set such that a statistical distribution of library members is produced in the absence of guest.

Simulated DCL for Fig. 3a and Fig. S2:

Building Block	Total concentration (M)
1	0.00333
2	0.00133

Library Member	*K*	Δ*G*°
9 (**1.1.1.1**)	1.0	-34.8
8 (**1.1.1**)	1.0	-28.0
7 (**1.1.2**)	3.0	-26.8
1.1	1.0	0.0
1.2.2	3.0	0.0
2.2.2	1.0	0.0
1.1.1.2	4.0	0.0
1.1.2.2	6.0	0.0
1.2.2.2	4.0	0.0
2.2.2.2	1.0	0.0

Simulated DCL for Fig. 4a:

Building Block	Total concentration (M)
1	0.01

Library Member	*K*	Δ*G*°
9 (**1.1.1.1**)	1.0	-34.8
8 (**1.1.1**)	1.0	-28.0
1.1	1.0	0.0

Simulated DCL for Fig. S1:

Building Block	Total concentration (M)
1	0.00333
2	0.00333
3	0.00333

Library Member	*K*	Δ*G*°
9 (**1.1.1.1**)	1.0	-34.8
8 (**1.1.1**)	1.0	-28.0
7 (**1.1.2**)	3.0	-26.8
1.1	1.0	0.0
2.3	2.0	0.0
1.2.2	3.0	0.0
2.2.2	1.0	0.0
1.1.3	3.0	0.0
1.3.3	3.0	0.0
3.3.3	1.0	0.0
1.2.3	6.0	0.0
1.1.1.2	4.0	0.0
1.1.2.2	6.0	0.0
1.2.2.2	4.0	0.0
2.2.2.2	1.0	0.0
1.1.1.3	4.0	0.0
1.1.3.3	6.0	0.0
1.3.3.3	4.0	0.0
3.3.3.3	1.0	0.0
2.2.2.3	4.0	0.0
2.2.3.3	6.0	0.0
2.3.3.3	4.0	0.0
1.1.2.3	12.0	0.0
1.2.2.3	12.0	0.0
1.2.3.3	12.0	0.0

REFERENCES

(S1) Otto, S.; Furlan, R.L.E.; Sanders, J.K.M. *J. Am. Chem. Soc.* **2000**, *122*, 12063.